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A COMPARISON OF CLINICAL FINDINGS IN FIFTY CASES OF NON-PARALYTIC POLIOMYELITIS WITH TWO OUTBREAKS OF ACUTE INFECTIVE ENCEPHALITIS, WHICH WERE NOT DUE TO ACUTE POLIOMYELITIS.

by

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PART ONE

Non-Paralytic Poliomyelitis.

The cases of acute non-paralytic poliomyelitis discussed here were admitted under my care to Brookfields Hospital, Cambridge, between the years 1947 to 1953. They occurred in association with cases of paralytic poliomyelitis admitted to the hospital over this period, and they were from areas in which paralytic poliomyelitis was prevalent at the same time.

Clinical Features of the Minor Illness.

44% of these cases gave a history of a "minor illness" preceding the onset of the major illness. The interval between the minor and major illness varied from one to seven days. The duration of the minor illness was, in the majority of cases, two to three days. The salient features of this prodromal illness were, fever, headache, general muscular pains and sore throat.

The occurrence of a biphasic pattern at the onset of acute poliomyelitis has been mentioned by numerous writers, including Hortsman (1949) and Ritchie Russell (1952).

The clinical features of the minor illness in the series under discussion were as follows:

Patients frequently complained that they had had a cold, but on further enquiry it was found that there was never any rhinorrhoea, and they did not suffer from an acute catarrhal exudate. There was in no case a history of swelling of the nasal mucous membranes sufficient to cause any distinctive nasal symptoms.

The sore throat complained of was never of such intensity as to cause pain or discomfort on swallowing and a cough was not a symptom in any of the cases. Generalised muscular pains were complained of by many of them.

It is only during an epidemic that attention is likely to be directed towards the occurrence of a minor illness. Cases of acute poliomyelitis admitted without a history of a minor illness afforded, therefore, an opportunity of studying the appearance of the nasopharynx in acute poliomyelitis.

The fauces and nasopharynx in such cases were found to be only slightly injected. There was no exudate to be seen and the throat and nose swabs were invariably negative on bacteriological examination.

Some of these patients had conjunctival injection and some had also palpable lymphatic nodes in the post-cervical region.

There were no positive findings that were characteristic of the minor illness. In fact, the absence of certain factors such as rhinorrhoea, cough, and local exudate, were of more significance.

Clinical Features of the Major Illness.

The most prominent symptoms (See also Fig.1.) were headache, nausea and vomiting, neck stiffness and pain, with stiffness of the back. The headache was not very intense and only seldom required analgesics. The mental condition was usually clear. Although the majority of them had vomited this was not a repeated or persistent symptom. In the majority of cases fever was present.

Neck and back stiffness featured as a symptom in about 50% of the cases. It was, however, a clinical finding in all of them. Although neck stiffness was

invariably present it was not, in the great majority of cases, very marked. I did not find any cases with visible head retraction, such as one finds in acute bacterial meningitis.

The meningism of acute poliomyelitis was of such a moderate character, in the vast majority of cases, that it was not obvious on looking at the patient. It was something that had to be searched for. It was present, however, so constantly in all cases that too much importance cannot be attached to this clinical finding. The incidence of various other symptoms is shown in Fig. 1.

It is worthy of mention that in no case did any convulsions occur. In 150 cases of paralytic poliomyelitis treated at Brookfields Hospital, over this same period, the absence of this feature was also noted.

Laboratory Investigations.

Lumbar punctures were performed in all 50 cases of non-paralytic poliomyelitis. The results of the findings are shown in Fig. 2. In order to obtain a more comprehensive picture of the cerebrospinal fluid, in acute poliomyelitis, the findings in 124 cases with paralysis which had lumbar punctures performed were analysed and the results are also shown in Fig. 3.

FIG. 1

NON PARALYTIC SYMPTOMS

50 cases

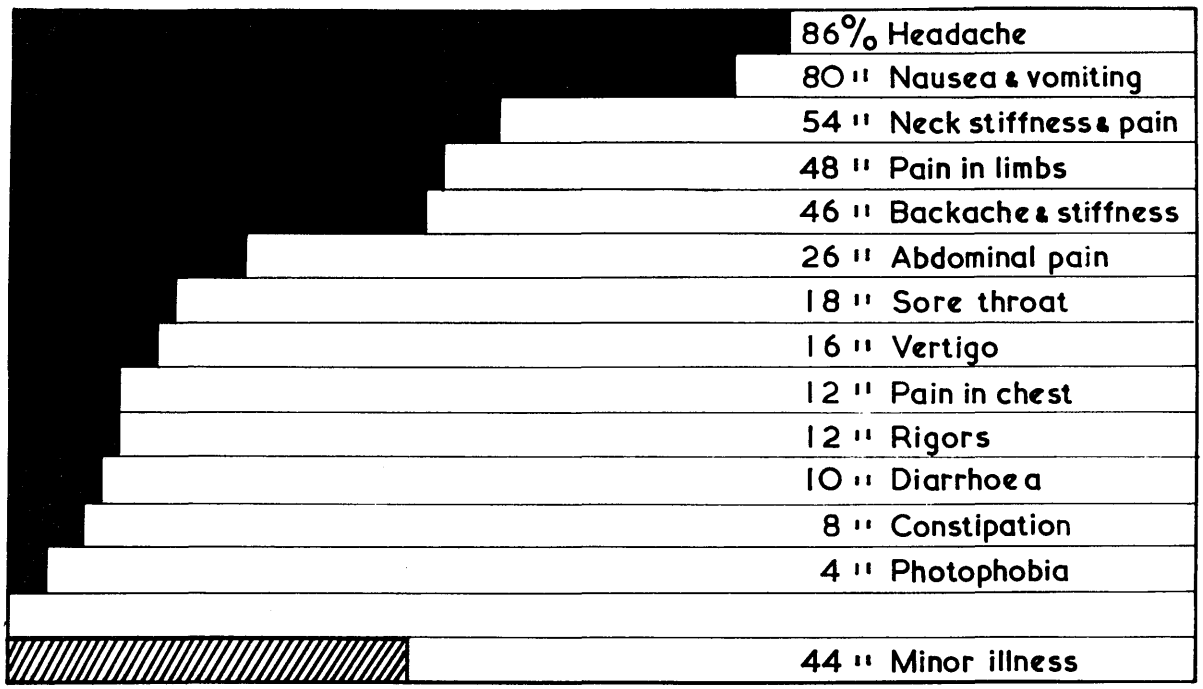


FIG. 2

Total cells 0 - 4			Total cells 5 - 9			Total cells 10 - 39			Total cells 40 - 99			Total cells 100 +		
Day of Illness	Granulocytes	Lymphocytes	Day of Illness	Granulocytes	Lymphocytes	Day of Illness	Granulocytes	Lymphocytes	Day of Illness	Granulocytes	Lymphocytes	Day of Illness	Granulocytes	Lymphocytes
2nd	0	3	5th	0	6	3rd	2	32	2nd	32	44	2nd	130	1300
3rd	0	4	6th	0	8	3rd	0	20	2nd	2	60	2nd	76	132
4th	0	3	6th	0	5	3rd	6	28	2nd	8	34	2nd	240	50
5th	0	3	7th	0	6	4th	8	26	2nd	68	28	2nd	24	186
5th	0	3				4th	10	20	3rd	25	60	3rd	98	22
						4th	1	7	3rd	22	40	3rd	44	64
						4th	6	20	3rd	9	49	3rd	5	170
						5th	2	10	3rd	18	25	3rd	95	100
						5th	16	20	4th	0	74	3rd	240	50
						6th	0	12	4th	48	30	3rd	92	36
						14th	0	19	4th	40	20	3rd	68	32
									5th	18	46	3rd	8	102
									5th	36	54	4th	74	26
									7th	18	78	4th	11	89
									7th	4	68	6th	12	294

RESULTS OF LUMBAR PUNCTURE ON 50 CASES OF NON-PARALYTIC POLIOMYELITIS

ANALYSIS IN RELATION TO TYPE OF CELL FOUND AND TIME OF PERFORMANCE OF LUMBAR PUNCTURE

FIG. 3

Total cells 0 - 4			Total cells 5 - 9			Total cells 10 - 39			Total cells 40 - 99			Total cells 100 +		
Day of Illness	Granulo-cytes	Lympho-cytes	Day of Illness	Granulo-cytes	Lympho-cytes	Day of Illness	Granulo-cytes	Lympho-cytes	Day of Illness	Granulo-cytes	Lympho-cytes	Day of Illness	Granulo-cytes	Lympho-cytes
3rd	0	3	4th	0	6	3rd	18	6	3rd	60	8	1st	280	110
4th	0	3	4th	0	8	3rd	12	4	3rd	56	18	2nd	138	114
5th	0	3	5th	0	6	3rd	7	12	3rd	70	20	2nd	138	132
5th	0	3	5th	0	6	3rd	27	12	3rd	0	90	2nd	84	26
5th	0	3	5th	0	6	4th	2	16	3rd	0	66	2nd	13	262
6th	0	3	7th	0	5	4th	12	27	3rd	0	60	2nd	348	38
6th	0	3	9th	0	8	4th	6	12	4th	0	74	3rd	104	254
7th	0	3	9th	0	8	4th	6	16	4th	0	58	3rd	22	88
7th	0	3				4th	4	24	4th	0	80	3rd	356	46
7th	0	4				4th	6	24	4th	0	47	3rd	380	20
8th	0	3				5th	0	30	4th	5	76	3rd	36	44
9th	0	3				5th	12	26	4th	0	80	3rd	20	80
12th	0	4				5th	0	26	5th	0	63	3rd	10	360
15th	0	3				5th	3	16	5th	12	48	3rd	25	140
						5th	4	32	5th	0	60	3rd	14	150
						5th	0	28	5th	0	55	3rd	26	142
						5th	5	24	5th	5	67	3rd	45	280
						5th	10	8	5th	12	85	3rd	14	96
						6th	4	14	5th	4	45	3rd	110	24
						6th	0	12	6th	18	28	4th	16	136
						6th	3	15	6th	2	72	4th	4	102
						6th	0	35	6th	0	60	4th	1	99
						6th	0	14	6th	0	50	4th	134	32
						6th	0	14	6th	0	48	4th	32	70
						7th	6	24	7th	8	70	4th	192	68
						7th	2	10	7th	0	40	4th	0	120
						7th	2	36	8th	0	72	4th	30	90
						8th	0	10				4th	148	226
						8th	2	24				4th	0	112
						9th	2	10				4th	14	274
						9th	0	12				5th	80	120
						11th	0	18				5th	70	174
						14th	0	10				5th	10	124
												5th	20	100
												6th	0	178
												6th	0	120
												6th	9	60
												6th	22	202
												7th	0	148
												7th	0	160
												7th	26	234
												8th	0	476

RESULTS OF LUMBAR PUNCTURE ON 124 CASES OF PARALYTIC POLIOMYELITIS

ANALYSIS IN RELATION TO TYPE OF CELL FOUND AND TIME OF PERFORMANCE OF LUMBAR PUNCTURE

Cell Counts.

In all instances the number of lymphocytes and granulocytes, as well as the protein and sugar concentrations, were determined. 10% of the non-paralytic series had a count of less than 5 cells/c.mm. The corresponding figure for the paralytic series was 12% (Fig.4).

FIGURE 4. C. S. FLUID CELL ANALYSIS.

CELL COUNT	NON-PARALYTIC		PARALYTIC	
	NUMBERS	PERCENTAGE	NUMBERS	PERCENTAGE
0 - 4	5	10	14	12
5 - 9	4	8	8	7
10 - 39	11	22	33	27
40 - 99	15	30	27	21
100 - 0	15	30	42	34
TOTAL	50	100	124	100

Of the non-paralytic series 8% had a count of 5 to 9 cells/c.mm. inclusive, the corresponding figure for the paralytic cases being 7%, and 22% had a cell count in the 10 to 39 group, the comparable percentage in the paralytic series being 27%.

In the group which had 40-99 cells there were 30% non-paralytic and 21% paralytic. Finally, 30% of the non-paralytic and 34% of the paralytic cases had cell counts of 100 or over.

The highest cell count in the non-paralytic series was 1430 (See Fig. 2) comprising 1300 lymphocytes and 130 granulocytes. The highest cell count in the paralytic series was 476, (Fig.3) composed entirely of lymphocytes.

Comment on Number of Cells Found in Cerebrospinal Fluid.

It is significant that in the non-paralytic and paralytic series 10% and 12% respectively had cell counts of less than 5. This is not in accord with Ritchie Russell's findings (1952), that the cerebrospinal fluid in the major illness is rarely normal. Nor does it agree with the statement of Beaumont (1953) that there is an excess of cells present (15 to 200 c.mm).

My finding is also at variance with that of Frazer (1913) that a cell count of over 10 should be regarded as abnormal, and those of Drury and Sladen (1939) who, in an analysis of 55 cases, concluded that the finding of a completely normal fluid practically excludes a diagnosis of acute poliomyelitis.

The cerebrospinal fluid findings in regard to cells and protein in this series are, however, in keeping with those of Paul(1951) that up to 12% in both non-paralytic and paralytic cases have persistently negative spinal fluids.

Types of Cell Found in the Cerebrospinal Fluid.

In the smaller counts, namely 10 and under, lymphocytes only were present. In cell counts over ten, 80% contained granulocytes in the non-paralytic series, and in the paralytic series 70% contained granulocytes.

In the non-paralytic series there was a preponderance of granulocytes over lymphocytes in only 18%, the corresponding figure in the paralytic series being 13.7%.

In this whole series of 174 cases, although granulocytes were present in 85%, the number of granulocytes exceeded the number of lymphocytes in only 15%.

The day of illness on which the lumbar puncture was performed is shown in Figs. 2 and 3. It will be noted from a study of these that the number of granulocytes exceeded the number of lymphocytes only when lumbar puncture was done within four days of the start of the major illness.

In the 50 cases of non-paralytic poliomyelitis there was seldom any clinical indication that the lumbar puncture should be repeated. It was found necessary to do so only on four occasions, and in each case there was no significant change in the lumbar puncture findings (See Fig. 5).

Lumbar puncture was repeated in four of the paralytic series and the changes found and the day of illness on which it was performed are shown in Fig. 6.

Protein. (Fig.7).

34% cases of non-paralytic poliomyelitis contained 40 mgm/100 ml. or less. 66% contained between 45 and 95 mgm/100 ml. 6% contained 100mgm/100 ml. or over.

The highest reading in the non-paralytic group was 130 mgm/100 ml.

27% of the paralytic poliomyelitis cases contained 40 mgm/100 ml. protein or less. 59% of the cases contained between 45 mgm. and 95 mgm/100 ml. protein and 14% contained 100 mgm/100 ml. or more. The highest reading in the paralytic cases was 225 mgm/100 ml.

FIGURE 5.

FOUR CASES OF NON-PARALYTIC POLIOMYELITIS

IN WHICH LUMBAR PUNCTURE WAS REPEATED

PATIENT	1st LUMBAR PUNCTURE	DAY OF ILLNESS	2nd LUMBAR PUNCTURE	DAY OF ILLNESS
B.D.	Cells < 3/cmm Protein 20 mgm/100 ml.	3rd	Cells 4/cmm Protein 20 mgm/100 ml	10th
G.M.	Cells < 3/cmm Protein 20 mgm/100 ml	3rd	Cells < 3/cmm Protein 20 mgm/100 ml	8th
J.K.	Cells 6/cmm Protein 45 mgm/100 ml	4th	Cells 3/cmm Protein 20 mgm/100 ml	10th
M.M.	Cells < 3/cmm Protein 30 mgm/100 ml	4th	Cells < 3/cmm Protein 20 mgm/100 ml	11th

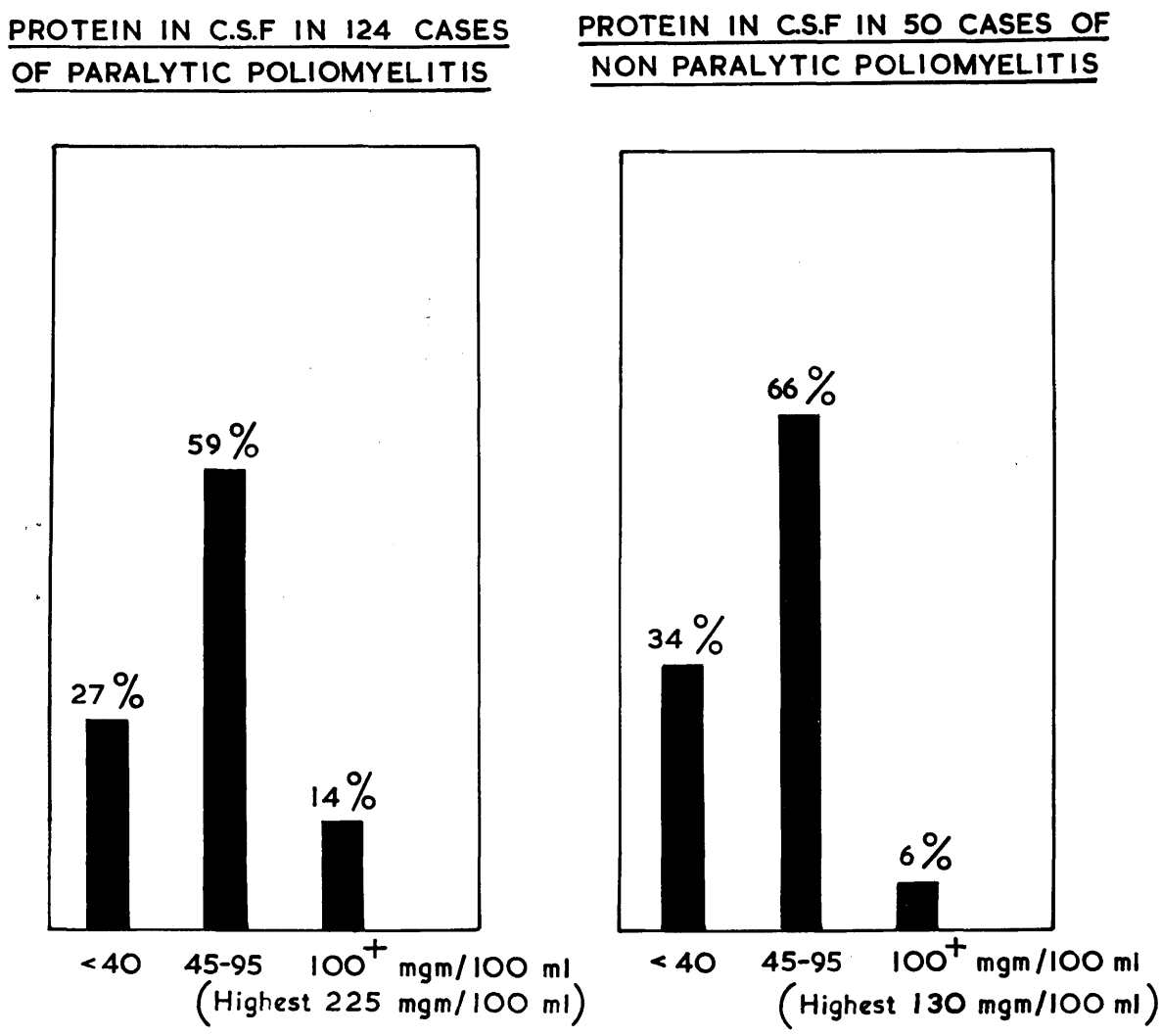
FIGURE 6.

FOUR CASES OF PARALYTIC POLIOMYELITIS

IN WHICH LUMBAR PUNCTURE WAS REPEATED

PATIENT	1st LUMBAR PUNCTURE	DAY OF ILLNESS	2nd LUMBAR PUNCTURE	DAY OF ILLNESS
J.F.	Cells <3/cmm Protein 30 mgm/100 ml	4th	Cells <3/cmm Protein 15 mgm/100 ml	8th
C.C.	Cells 74/cmm Protein 60 mgm/100 ml	5th	Cells <3/cmm Protein 120 mgm/100 ml	21st
H.M.	Cells 360/cmm Protein 200 mgm/100 ml	8th	Cells 141/cmm Protein 200 mgm/100 ml	10th
C.P.	Cells 140/cmm Protein 70 mgm/100 ml	4th	Cells 19/cmm Protein 65 mgm/100 ml	7th

FIG. 7


PROTEIN IN C.S.F IN 124 CASES OF PARALYTIC POLIOMYELITIS
27 %
59 %
14 %
< 40
45-95
100+ mgm/100 ml
(Highest 225 mgm/100 ml)
PROTEIN IN C.S.F IN 50 CASES OF NON PARALYTIC POLIOMYELITIS
34 %
66 %
6 %
< 40
45-95
100+ mgm/100 ml
(Highest 130 mgm/100 ml)

In neither the non-paralytic nor the paralytic cases was the protein content markedly increased. In only 6% non-paralytic and 14% paralytic was the reading 100 or over (Fig. 7). In a considerable proportion, 34% non-paralytic and 27% paralytic, the protein content of the cerebrospinal fluid was 40 mgm/100 ml. or below. In 66% of the non-paralytic and 59% of the paralytic cases the protein content varied from 45 mgm to 95 mgm/100 ml.

Various authorities differ in their interpretation of the normal protein content of the cerebrospinal fluid. Brain (1951) quotes the figure of 20-40 mgm/100 ml. Paul (1951) quotes any reading above 35-45 mgm/100 ml. as being abnormal. Henderson and de Guttierey-Mahoney(1950) state that they regard any reading up to 60 mgm/100 ml. as being within normal limits.

As a result of an analysis of about 1000 lumbar punctures performed by the writer at Brookfields Hospital, in the last 15 years, it is considered that a reading of over 40 mgm/100 ml. should be regarded with suspicion and warrants some explanation.

It must be remembered that in the estimation of the protein content of the cerebrospinal fluid, there is a considerable margin of error owing to the calorimetic nature of the test. (Personal communication from Dr.Gleeson White, University Bacteriologist to Addenbrooke's Hospital).

Conclusions to be drawn from investigation of the Cerebrospinal Fluid in 174 cases of Acute Poliomyelitis.

1. 11% recorded no abnormality in the cerebrospinal fluid as regards cell or protein content.

2. Granulocytes and lymphocytes were present together in 60% of the cases.

3. In 15% of the cases there was a preponderance of granulocytes over lymphocytes. The preponderance was only found when a lumbar puncture was performed within four days of the commencement of the major illness.

4. The increase in protein was only moderate.

5. The sugar content of the cerebrospinal fluid was within normal limits in every case.

6. An estimation of the chlorides content done in 65% of the cases showed this to be within normal limits in each case.

Blood Examination.

A total and differential white cell count was done in 24% of the non-paralytic cases. The results are shown in Fig. 8.

FIGURE 8.

DIFFERENTIAL WHITE CELL COUNT IN 12 CASES OF NON-PARALYTIC POLIOMYELITIS.

NAME	AGE	TOTAL COUNT	% OF LYMPH
J.M.	5 yrs	16,400	13.0
J.W.	32 "	9,500	14.5
T.Y.	11 "	6,600	34.0
S.T.	9 "	6,300	24.5
M.Y.	19 "	9,900	15.5
M.P.	6 "	6,000	12.0
J.W.	38 "	8,000	23.0
D.S.	5 "	13,000	5.5
P.P.	$4\frac{1}{2}$ "	6,900	31.5
R.B.	7 "	5,300	17.0
D.B.	3 "	13,000	21.0
F.K.	21 "	4,200	19.0

The total white cell count in three of these cases was over 10,000. The lowest total white cell count was 4,200. The percentage of lymphocytes varied from 5.5% to 34%.

PART TWO

Clinical Findings in 11 Cases of Acute Infective Encephalitis Occurring in the Village of Bourn, Cambridgeshire.

This outbreak occurred in the latter half of October and early November 1955.

The first case occurring was that of M.B., a boy aged 5 years, who was admitted to Addenbrooke's Hospital, Cambridge, on the 22nd October (See Fig. 9). The case history showed an illness of five days duration. He complained of backache, vomiting, headache and sore throat. A lumbar puncture was performed at this hospital. The cerebrospinal fluid contained 436 lymphocytes/cm. 36 granulocytes/cm, protein 60 mgm/100 ml., sugar 57 mgm/ml. He was detained in hospital for 5 days, then being sent home. On the 25th October, there was admitted to Addenbrooke's Hospital, from the same village, R.C., a baby of 6 months. This baby had been ill since the 22nd October, with fever, vomiting and general malaise. A lumbar puncture was performed. The spinal fluid contained 730 lymphocytes per cu.mm., 48 granulocytes per cu.mm., protein 70 mgm/100 ml., sugar 57 mgm/100 ml. His condition improved rapidly and he was discharged from hospital on the 28th October.

The clinical details of these two cases, M.B. and R.C., have been obtained from the records at Addenbrooke's Hospital, through the courtesy of Dr.Douglas Gairdner, Consultant Paediatrician at the hospital.

On October 28th, M.M., a girl of 12 years of age, was admitted to Brookfields Hospital, suffering from acute infective encephalitis. Two days later, on the 30th October, her mother Mrs. I.M., aged 37 years, was admitted with a similar illness.

On the 6th November five cases were admitted to Brookfields Hospital with signs and symptoms of acute infective encephalitis. The history of these cases, admitted on the 6th November, indicated direct or indirect contact with the two cases of acute infective encephalitis admitted to Addenbrooke's Hospital on the 22nd and 25th October, (Fig. 9).

Two of the cases admitted on November 6th were nurses from Addenbrooke's Hospital who had nursed M.B. and R.C., when these children were patients in the Children's Ward there from the 22nd to the 28th October.

The remaining three cases admitted on the 6th November came from the Bourn area. Two of them were brothers, G.R. and L.R., aged 17 years and 15 years respectively.

FIGURE 9.

CLINICAL FINDINGS IN 11 CASES OF ACUTE INFECTIVE ENCEPHALITIS AT BOURN IN 1955.

NAME	AGE Yrs	DATE OF ONSET	DATE OF ADMISSION	HEAD-ACHE	VOMIT-ING	BACK-ACHE	SORE THROAT	LIMB PAINS	PHOTO-PHOBIA	MENIN-GISM	BIPH-ASIC	TEMP ON ADMISSION
M.B.	5	17/10	22/10	+	+	+	+	-	-	+	-	99.8°
R.C.	6/12	22/10	25/10	±		±	-	-	-	+	-	102.0°
M.M.	12	26/10	28/10	+	+	+	+	-	-	+	-	101.6°
I.M.	37	28/10	30/10	+	+	-	-	-	-	+	-	101.6°
C.W.	20	30/10	6/11	+	+	+	-	-	-	+	-	100.0°
E.K.	23	31/10	6/11	+	+	+	-	+	-	+	+	101.8°
G.R.	17	3/11	6/11	+	+	+	+	-	+	+	-	103.0°
L.R.	15	5/11	6/11	+	-	+	-	-	+	+	-	103.6°
L.M.	10	5/11	6/11	-	+	+	-	-	-	+	-	102.0°
H.CM.	29	8/11	9/11	+	-	-	-	-	-	+	-	102.0°
R.K.	26	11/11	12/11	-	-	-	-	+	-	+	-	102.0°

The further admission on the 6th November was L.M., a member of the M. family, also from Bourn, her sister M.M. and her mother I.M. having been admitted to Brookfields Hospital on the 28th and 30th October respectively.

There was a further admission from Bourn on the 9th November, Mr. H.C.M., aged 29 years, who lodged with the R. family, the two R's, L.R. and G.R., having been admitted on the 6th November.

The last admission of this group of cases was Mr.R.K., aged 26 years, who was admitted on the 11th November. He was the husband of Mrs. E.K., one of the nurses who had attended the original two patients admitted to Addenbrooke's Hospital.

Headache, backache and vomiting, were the most common symptoms complained of. Other symptoms, less prevalent, were sore throat, limb pains and photophobia.

A biphasic element was noted in the case of Mrs.E.K. All the patients had a raised temperature on admission, varying from 99.6° to 103.6°. All had signs of meningism, with stiff neck, spinal and hamstring spasm. Two of them had nystagmus. None had any muscular weakness. No sensory

changes and no character changes were noted. Tendon reflexes were increased. No other abnormality of the central nervous system was found.

Laboratory Investigations (See Fig. 10).

All the cases showed abnormalities in the cerebrospinal fluid, the lymphocytes being increased in all cases. The granulocytes were increased in 8 of the 11 cases.

FIGURE 10 RESULTS OF AN INVESTIGATION OF 11 CASES OF ACUTE INFECTIVE ENCEPHALITIS AT BOURN.

NAME OF PATIENT	DAY OF ILLNESS	CEREBROSPINAL FLUID				BLOOD			POLIO VIRUS IN FAECES
		GRAN	LYM-PH	PRO-TEIN	SUG-AR	TOTAL LEUC.	% LYMPH	PAUL BUNNELL	
M.B.	5	26	436	60	57	NOT	TESTED	-	-
R.C.	3	48	730	70	57	5700	47	-	-
M.M.	3	40	502	70	51	5000	26	-	-
I.M.	3	3	10	50	50	11000	20	-	-
C.W.	3	6	174	55	50	3400	25	-	-
E.K.	7	3	140	95	64	NOT TESTED	-	NOT TESTED	-
G.R.	4	6	72	55	56	6300	37	-	-
L.R.	(2	3	3	35	53	7200	6	-	-
	(7	21	267	55	65	5400	45		
L.M.	2	10	14	35	75	5800	24	-	-
H.D.M.	2	6	30	55	64	NOT TESTED	-	NOT TESTED	-
R.K.	3	30	1180	170	66	11000	10	-	-

In the case of the patient L.R., a lumbar puncture performed on the second day of his illness revealed no abnormality. The lumbar puncture was repeated on the seventh day of his illness when there was a total count of 288 cells per cu.mm., of which 267 were lymphocytes.

The highest number of lymphocytes found in the cerebrospinal fluid in this series was 1180, from a lumbar puncture performed on the third day of illness. The lowest lymphocyte count was 10, lumbar puncture in this case also being performed on the third day. The highest granulocyte count was 48 per cu.mm., and in three cases less than 3 granulocytes per cu.mm. were found. In no case was there a preponderance of granulocytes over lymphocytes.

In 10 of the 11 cases the cerebrospinal fluid protein was raised. In only one case was it over 100 mgm/100 ml., a reading of 170 mgm/100 ml. The sugar content of the cerebrospinal fluid was within the normal limits in all cases.

A total white and differential blood count was done in eight of the eleven cases. The highest total count was 11,000 (in two cases). The percentage of lymphocytes in the peripheral blood varied from 6% to 47%. A Paul Bunnell test was negative in all of the eight cases on which a differential white blood count was done. The erythrocyte sedimentation

rate was examined in six of the cases. In the case of the patient L.M., there was a marked increase to 30, otherwise the increase was slight.

Virus Investigation.

Faeces from all the Bourn cases yielded negative results for poliomyelitis virus, and for the Coxsackie group of viruses. One of the E.C.H.O. group of viruses, however, was isolated from four of the Bourn cases.

The method used was essentially that described by Zitcer et al (1955). Foetal membranes from which the placenta had been removed were placed aseptically in sterile screw-capped jars and these were held at 4°C in a refrigerator until used. Where possible, membranes were used less than 10 hours after delivery but, occasionally, satisfactory results were obtained with membranes stored for 18 hours.

The amnion was stripped from the chorion, cut into pieces 1 inch square, washed to remove excess mucus and blood with cold phosphate buffered saline (PBS) (Dulbecco and Vogt, 1954) and treated with successive 40 ml. aliquote of 0.25% Difco trypsin in PBS, previously warmed to 37°C. The system was maintained at 37°C on a warm plate and agitated with a magnetic stirrer. Every 15 minutes the supernatant which contained epithelial cells which had separated from the amnion sheets

was poured off into a 200 ml. centrifuge bottle which was cooled in an ice bath. Fresh trypsin was then added to the amnion. A total of 6 such trypsinations was carried out. The suspensions containing epithelial cells were pooled and the whole was centrifuged at 100 r.p.m. for 10 minutes in a horizontol centrifuge. After washing once in PBS the cells were suspended in 10 ml. of a medium containing 20% human serum and 0.5% lactalbumin hydrolysate in Gey's (1949) balanced salt solution. After a cell count was made the cell suspension was diluted with the same medium so as to contain not less than 500,000 cells per ml. 1 ml. quantities were pipetted into 5 x $\frac{5}{8}$" pyrex tubes which were stoppered with silicone bungs and incubated stationery at 37°C inclined at 5° from the horizontal.

After three days' incubation at 37°C sheets of epithelial cells had begun to spread over the glass surface. The medium was poured off and replaced by 1 ml. of a medium containing 10% normal rabbit serum (previously heated at 60°C for 20 minutes) and 0.5% lactalbumin hydrolysate in Gey's solution. After a further three days' incubation, a confluent sheet of flattened cuboidal cells with clear cytoplasm and large rounded or oval nucleus had formed. The cells were now ready for inoculation with virus.

Immediately prior to inoculation, the cultures were washed twice with Gey's solution. Finally, 1 ml. quantities of a maintenance medium consisting of 5% normal rabbit serum and o.25% lactalbumin hydrolysate in Gey's solution were added to each tube and the virus inoculation was made into this fluid. Uninoculated cultures remained intact in this maintenance medium for at least five days.

All media which were used during the growth and maintenance of the tissue cultures contained penicillin 100 units per ml. streptomycin 100 per ml. and Nystatin (Squibb) 40 units per ml.

Isolation of Virus from Faeces or Rectal Swabs. Faeces were collected less than one week after onset of illness and were stored in screw-capped jars at -20°C. After thawing, a $\frac{1}{2}$" pellet of faeces was ground in a sterile mortar and extracted with 10 ml. of cold PBS. The suspension was centrifuged at 8000 r.p.m. for 25 minutes in an angle centrifuge, the head of which was previously cooled at -20°C. The clear supernatant which was now free of bacteria was stored in screw-capped bottles at -20°C.

Rectal swabs were extracted with 2 ml. of maintenance medium. The extract was centrifuged and stored in the same manner as the faecal extracts.

Faecal extract in 0.1 ml. aliquots was inoculated into each of the two culture tubes containing 1 ml. of maintenance medium. The cultures were observed daily for 5 days. When more than half the cells were rounded up, with shrunken nuclei and opaque, granular cytoplasm, so that the sheet of cells was disrupted, it was considered likely that virus was present in the faecal extract. The supernatant fluids were harvested, pooled and stored at -20°C to await further identification. Cytopathogenic effects were usually well developed on the third or fourth day.

Typing of virus strains. Virus strains were typed according to the method of Syverton (1956) using eight tubes of human amnion cultures. Type specified antisera prepared in monkeys against poliomyelitis types 1, 11 and 111 which were used, were obtained through the courtesy of Dr. D.G.ff. Edward.

Titration of virus. Serial tenfold dilutions of first or second passage virus in tissue culture fluid were made in maintenance medium. 0.1 ml. aliquots of these dilutions were inoculated into each of two tubes. The tubes were observed daily for 4 days. One tissue culture infective dose (TCD) was the reciprocal of the highest dilution of stock virus which caused advanced cytopathogenic effects in one or both culture tubes after inoculation of 0.1 ml.

Neutralisation test. Serum samples which were obtained from patients and contacts were stored at -20°C until tested. Serial fivefold dilutions of serum were made in Mixture 199 (Morgan et al. 1949) or Gey's solution commencing at 1/10. An equal quantity of virus, diluted in maintenance medium to contain 1000 TCD was added. The serum-virus mixtures were held at room temperature for between 15 and 45 minutes after which 0.75 ml. aliquots were added to each of two culture tubes from which all fluid had been removed. The tubes were observed daily for 4 days. Virus controls and uninoculated cultures were always included in every test. The titre of the serum was expressed as the reciprocal of the highest dilution which caused inhibition of cytopathogenic effect in one or both culture tubes.

VIRUS ISOLATIONS

Virus was isolated from the faeces of two patients L.M., and L.R. by inoculation of human amnion cell cultures with extracts of faeces obtained on the second and third day of illness respectively. These two viruses behaved similarly in tissue culture and serologically they were indistinguishable (Fig.11). From the same stool specimen taken from L.R. on the third day of illness, virus was isolated in the cultures

of monkey kidney cells. Using monkey kidney cultures, Dr. G. P. B. Boissard of the Virus Reference Laboratory, Colindale, isolated virus from faeces of patients E.K. taken on the 6th day of illness and from C.W. on the 7th day. These viruses were antigenically similar to virus isolated from L.R.

Faeces were obtained from six other patients between 3 and 7 days after onset of illness. No virus was isolated when faecal extracts were inoculated into human amnion cultures. (Figure 12). No specimen of faeces was available from M.B., the first patient of the series.

The virus which was isolated from patient L.R. has been named "Bourn virus strain L.R." For most of the tests to be described in this paper, the seed virus was tissue culture fluid either from its first passage in human amnion cultures or from its second passage in monkey kidney cultures. The isolation in monkey culture was made at a time when only well characterised viruses were being used in the laboratory, and it was not due to contamination with any of these agents. The isolation in human amnion culture was made 3 months later from the same faecal extract. In human amnion cultures some cytopathogenic effect was observed on the third day after inoculation of faecal extract and this was complete on the fourth day. In subsequent passages, complete cytopathogenic

effect was observed on the second day. The cytopathogenic effect was indistinguishable from that caused by poliomyelitis virus (Fig. 11). The titre of first and second amniotic passage virus was $10^{-6.0}$ in human amnion culture. In monkey kidney culture cytopathogenic effect was complete on the second day in the case of both primary isolation, second passage and third passage. The titre of second passage virus was $10^{-6.0}$ in both monkey kidney and human amnion cultures.

Bourn virus in second amniotic passage passed through a Seitz EK filter without loss of titre. Virus in first amniotic passage and second monkey kidney passage has been stored at -20°Z without loss of titre for over three months, despite repeated freezing and thawing. Some infectivity was preserved by lyophilisation in a centrifugal freeze drier, but the titre was reduced about 10^4 times.

Strains of Bourn virus which were isolated from L.R. and L.M. were not neutralised by antiserum prepared against poliomyelitis types 1, 11 and 111. Strain was not neutralised by antisera to types A_2, A_3, A_4, A_5, A_6, A_9, B_1, B_3, B_4, and B_5, Coxsackie viruses. These Coxsackie antisera were kindly supplied by Dr. D.A.J. Tyrrell. The strains of virus which

FIGURE 11. SEROLOGICAL RELATIONSHIPS OF VIRUSES ISOLATED FROM CASES OF ASEPTIC MENINGITIS.

NAME OF PATIENT	DAYS AFTER ONSET	SERUM TITRE AGAINST STRAIN OF VIRUS FROM EACH PATIENT	
		L.R's SERA:	HOMOLOGOUS SERA:
L.R.	3	<10 * 50 +	<10 * 50 +
L.M.	2	<10 >100	<10 >100
E.K.	6	<10 250	50 >250
C.W.	7	<10 >50	50 50
B.M.	NOT ILL	<10 >50	<10 >250
A.D. ‡	3	<10 >50	250 250

* Titre of "Acute" serum.

\- Titre of "Convalescent" serum.

‡ Single case which occurred in another village 2 months after Bourn cases.

FIGURE 12. NEUTRALISATION TESTS AGAINST BOURN VIRUS.

CASES				CONTACTS		
NAME	Virus isolation in faeces (strain)	Days after onset	Antibody titre against Bourn Virus	NAME	Days after first case	Antibody titre against Bourn Virus
M.B.	NOT TESTED	7 20	250 250	B.M.	23 43	10 50
R.C.	0	4 16	50 250	H.Z.B.	24 49	10 10
M.M.	0	5 20	250 250	R.O.C.	23 43	100 100
I.M.	0	3 16	50 250	E.A.C.	23 43	10 10
C.W.	+ ✱	6 18	250 250	P.L.	23 43	100 100
E.K.	+ ✱	5 17	10 50	D.L.	23 43	100 100
G.R.	0	5 18	10 250	E.R.R.	23 43	100 100
L.R.	+	3 16	10 50	J.R.	23 43	100 100
L.M.	+	2 13	10 250	P.R.	23 49	10 50
H.D.M.	0	3 13	10 250	B.R.	21	10
R.K.	0	5 14	250 250	A.R.	21	10
				A.C.	27	50
				L.C.M.	23	10
				B.B.	24	50

✱ Isolated in monkey culture by Dr. G.P.B. Boissard.

0 Bourn virus isolated from a rectal swab collected on this date.

were isolated from patients E.K. and C.W. were not neutralised by poliomyelitis antisera types I, II and III (Boissard, personal communication).

Lyophilised Bourn virus was sent to Dr. J. L. Melnick of Yale University, Section of Preventive Medicine. He has reported that Bourn virus belongs to the E.C.H.O. group of virus type 9.

Inoculation of 10^5 infective doses of human amniotic and monkey kidney passage virus failed consistently to cause any cytopathogenic effect in cultures of human epithelial cells strain HeLa.

A total of 11 litters of newborn mice have been injected intracerebrally with Bourn virus strain L.R. Each mouse received 10^4 TCD of virus suspensions in maintenance medium. Deaths which occurred before the 4th day after inoculation were not considered due to virus. One or more mice in each of 5 litters remained normal for at least 11 days after injection. In each of 6 litters some mice were found dead between 5 and 11 days after injection, but these mice were not sick on the previous day. Between the 6th and 10th day after injection 8 mice which came from 6 litters showed generalised wasting and weakness in one or more limbs one

day before death. Virus concentration was high in the torsos of sick mice but low in the brains. Passage of torso suspension intracerebrally to other newborn mice at 10^{-1} dilution caused wasting and limb paralysis in 4 mice out of 6 belonging to one litter 9 to 10 days after injection. Virus was present to high titre in the torsos of these mice.

A total of 10 litters of newborn mice were injected intracerebrally with maintenance medium only. All mice in 5 litters died between 2 and 7 days after inoculation, but some mice in the remaining 5 litters survived at least 11 days.

Histological sections were prepared from brain and anterior abdominal wall of mice 5 to 10 days after inoculation of Bourn virus. No changes suggestive of infection with Coxsackie virus were detected.

No illness was produced following inoculation of Bourn virus into weaned mice 3 to 4 weeks old either by the intracerebral or the intraperitoneal route. No lesions were detected following inoculation ofBourn virus into the yolk sac or on the chorioallantois of fertile hen eggs.

Although the Bourn virus belongs to the E.C.H.O. group it may produce weakness and paralysis in a few newborn mice after injection of large amounts of virus, but this ability to cause illness in mice did not increase after two mouse passages.

NEUTRALISATION TESTS

Paired sera were obtained from all 11 clinical cases. Early sera were collected between 2 and 7 days after onset and late sera were obtained 13 to 20 days after onset. Neutralisation tests were performed on these sera, using 1000 TCD of Bourn virus (Fig. 12). Seven cases showed a fivefold or greater increase in neutralising antibody titre between the first and second serum samples. Five of these seven cases had no antibody in the first serum, but two had titres of 50 on the third and fourth days of illness. The remaining four cases whose sera showed no rising titre all had a titre of 250 or greater when they were bled. Initially on the 5th, 6th or 7th day of illness.

Sera were obtained from 14 family contacts of the Bourn cases 23 days after the first case occurred. Of these, 8 had a neutralising antibody titre of 50 or greater, in two the titre was 10, and 4 sera had no antibody (Fig. 12). Further serum samples were obtained from 9 of these subjects 43 days after the first case occurred. None of these subjects had been ill meanwhile. In 7 subjects the antibody titre was unchanged. Two subjects B.M. and P.R. had no antibody in the first serum sample, but antibody was detected in the second sample. Bourn virus was isolated from a rectal swab which was

was taken from B.M. at the time the first serum sample was collected but no virus was detected in a rectal swab taken from P.R.

Attempts were made to isolate virus from faeces of four other patients who were admitted to hospital at the same time as the Bourn cases. Two of these were diagnosed clinically as suffering from non-paralytic poliomyelitis. Type I poliomyelitis virus was isolated from both cases. No antibody to the Bourn virus was detected in acute or convalescent sera taken from either patient. The other two cases were diagnosed as suffering from aseptic meningitis, but neither had contact with the Bourn cases. No virus was isolated from the faeces of either case, but one patient had a rising titre of antibody to Bourn virus and the other patient had antibody in both the acute and convalescent sera.

Virus isolations were attempted from faeces of 16 patients who were admitted to Brookfields Hospital between 1st January and 31st July 1956. Human amnion cultures were always used. Amongst the 6 patients who suffered from aseptic meningitis, virus was isolated from one case, A.D. This virus was not poliomyelitis but serologically it was related to Bourn virus (Fig. 12). Of the four patients who were admitted with

non-paralytic poliomyelitis, all were excreting type III poliomyelitis virus in the stools. In the group of 6 patients with paralytic poliomyelitis, type III poliomyelitis vrius was isolated from three patients and type I poliomyelitis virus was isolated from another two patients.

PART THREE

AN OUTBREAK OF ACUTE INFECTIVE ENCEPHALITIS AT BISHOP'S STORTFORD, HERTS, IN OCTOBER/NOVEMBER 1956.

This outbreak of acute infective encephalitis occurred in the town of Bishop's Stortford in Hertfordshire, about 35 miles from Cambridge, and ten of the cases came under my immediate care. The clinical findings are summarised in Fig. 13. It is interesting that this outbreak occurred at an almost identical time of the year to the Bourn epidemic in the previous year.

The first two admissions were C.J.B., a boy of 7 years of age, and his sister S.B. aged 3 year. They were both taken ill on the 24th October.

Two days later, on the 30th October, D.B., a girl 12 years of age, a cousin of the C.J.B. and S.B. was admitted with similar symptoms. They lived in adjacent houses. The remainder of the children admitted later attended the same school.

There were two adults, Mrs. M.F. aged 40 years, who was the mother of N.F. aged 12 years, admitted with her son on the 2nd November, and Mrs. E.R. aged 25 years, admitted on the 6th November.

FIGURE 13 CLINICAL FINDINGS IN 10 CASES OF ACUTE INFECTIVE ENCEPHALITIS AT BISHOP'S STORTFORD IN 1956.

NAME	SEX	AGE Yrs	DATE OF ONSET	DATE OF ADMISSION	HEAD-ACHE	VOMIT-ING	BACK-ACHE	SORE THROAT	LIMB PAINS	PHOTO-PHOBIA	MENIN-GISM	BIPH-ASIC	TEMP ON ADMISSION
J.P.	M	5	5/11	8/11	+	-	-	+	+	+	+	+	99.0°
N.R.	M	14	1/11	6/11	+	-	+	-	-	+	+	-	101.2°
P.P.	M	8	26/10	1/11	+	+	+	-	-	-	+	+	102.2°
M.F.	F	40	31/10	2/11	+	+	+	-	+	+	+	-	100.2°
E.R.	F	25	5/11	6/11	+	+	-	-	-	+	+	-	98.6°
N.F.	M	12	30/10	2/11	+	+	-	-	-	+	+	-	101.4°
J.W.	F	5	28/10	2/11	+	+	-	+	+	-	+	+	100.0°
C.J.B.	M	7	24/10	28/10	+	-	+	+	-	-	+	-	101.2°
S.B.	F	3	24/10	28/10	+	+	-	-	+	-	+	-	98.0°
D.B.	F	12	26/10	30/10	+	+	+	+	+	-	+	+	101.0°

Symptoms and Clinical Findings.

Headache, backache, vomiting, limb pains and photophobia were the most prominent features. Four of the ten patients complained of sore throat, and in another four there was a biphasic pattern in the history. With one exception, S.B., the temperatures were raised on admission.

All ten cases had signs of meningism, nuchal spasm, spinal and hamstring spasm. Three of the ten had nystagmus. None had any muscular weakness, or sensory changes. No behavious abnormalities were observed.

Investigations (Fig. 14).

Spinal fluid abnormalities were found in the nine cases on which a lumbar puncture was performed. Lymphocytes were increased in all cases, the highest count being 780 per cu.mm. in the case of N.F. The lowest lymphocyte count was 22. In two cases E.J.B. and D.B., there was a preponderance of granulocytes over lymphocytes. In these two cases the lumbar puncture was done on the 4th day of illness.

The highest granulocyte count was 198 per cu.mm. The protein was raised in five cases, the highest recording being only 65 mgm/100 ml.

The sugar content was within normal limits in all cases. The results of total white and differential blood counts are shown in Fig.14.

The maximum total leucocyte count was 9,400, the minimum 4,400. The percentage of lymphocytes ranged from 15% to 45%. The routine Paul Bunnell test was negative in each case and the erythrocyte sedimentation rate varied from 6 to 22. Faeces in all cases were negative for poliomyelitis virus isolation.

FIGURE 14 RESULTS OF AN INVESTIGATION OF 10 CASES OF ACUTE INFECTIVE ENCEPHALITIS AT BISHOP'S STORTFORD.

NAME OF PATIENT	DAY OF ILLNESS	CEREBROSPINAL FLUID				BLOOD				POLIO VIRUS IN FAECES
		GRAN	LYMPH	PROTEIN	SUGAR	TOTAL LEUC.	% LYMPH	PAUL BUNNELL	ESR	
J.P.	4	16	220	50	56	6500	26	-VE	9	-
N.R.	5	20	280	50	64	6100	26	-VE	10	-
P.P.	5	198	200	45	56	6400	42	-VE	22	-
H.F.	6	2	126	65	51	4500	27	-VE	5	-
E.R.	2	0	52	40	33	4400	15	-VE	10	-
N.F.	3	20	780	60	62	8400	30	-VE	17	-
J.W.	5	0	22	30	48	NOT DONE		NOT DONE		-
E.J.B.	4	170	102	35	88	NOT DONE		NOT DONE		-
S.B.	5	NOT DONE		NOT DONE		9400	45	-VE	21	-
D.B.	4	72	38	40	78	6300	20	-VE	6	-

DISCUSSION

The clinical features of 50 cases of acute poliomyelitis have been presented together with comparable clinical findings of two separate outbreaks of acute infective encephalitis, not due to acute poliomyelitis. In the literature we find similar evidence, for example, Galpine and Macrae (1953) describe an outbreak of benign meningo-encephalitis occurring in the Coventry district in the Summer of 1951. The number of cases of paralytic poliomyelitis quoted as being admitted to the Coventry Hospital for 1951 was 14, whereas 112 patients were admitted with symptoms and signs of benign meningo-encephalitis. Ninety of these had an abnormal cell count in the cerebrospinal fluid with or without increase of protein. A further nine showed an increase in the cerebrospinal fluid protein content of 60-80 mgm/100 ml. The peak months of their occurrence was May to July, with a sharp drop at the end of July. The authors state that multiple cases in one family were probably not uncommon. They quote the case of a girl of 11 year of age with meningeal signs and a cerebrospinal fluid cell count of 140. About the same time all other four children in the family were ill, but nursed at home. The virological investigations undertaken were on a limited scale.

Virus investigations for poliomyelitis were negative, but one of the Coxsackie viruses was isolated. They concluded that a Coxsackie virus may have caused a proportion of the benign encephalitis illness which they described.

Wallis (1955) described a similar epidemic occurring in Cumberland from January to April 1955. The signs and symptoms in the few clinical records described, would suggest an acute infective encephalitic illness. All had pyrexia, headache, backache, nausea, neck stiffness and conjunctivitis. A lumbar puncture was not performed in any of these cases. A feature of this outbreak was that multiple cases occurred in each household. Virus investigations up to the time of the report of this epidemic in August 1955 had been negative.

The cases described by Galpine and Macrae, and by Wallis, present a clinical picture similar in many respects to the Bourn and Bishop's Stortford outbreaks. A feature common to all of them is the frequency with which multiple cases in the one household occurred.

The Cumberland epidemic described by Wallis occurred at a time when there was no poliomyelitis in the district. There was evidence of a virus infection causing local upper respiratory and conjunctival infection and presumably also encephalitis.

The epidemic at Coventry resembles very closely the Bourn and Bishop's Stortford epidemics. This epidemic occurred at a time when some cases of paralytic poliomyelitis were admitted to the same hospital.

Huston et al (1956) encountered a large number of non-paralytic poliomyelitis cases in Surrey in the Autumn of 1955. A strain of orphan virus as well as poliomyelitis virus types 1 and 3 were isolated.

By contrast the results of a clinical study of 93 cases of encephalitis occurring in the Newcastle-upon-Tyne area, from 1946-1954 do not suggest the occurrence of epidemics similar to Bourn and Bishop's Stortford (Brewis 1954).

The presence of viruses other than that of poliomyelitis virus, during epidemics of that disease, has been demonstrated by various virologists. Dalldorf (1952) found the presence of Coxsackie viruses during epidemics of poliomyelitis in each year for a five-year period up to 1952 in New York City. Melnick and Kaplan (1950) found poliomyelitis virus and Coxsackie virus in 16% of the specimens of faeces collected from poliomyelitis in-patients. Curnen (1948) states that illnesses attributed to Coxsackie viruses have taken the form of non-paralytic poliomyelitis in Connecticut and Rhode Island

in 1948. He quotes 157 patients who were admitted to hospital with a diagnosis of poliomyelitis or aseptic meningitis and regarded the high incidence of non-paralytic cases as statistically significant. 72% were classified as non-paralytic. The highest incidence of those without paralysis was in August, whereas the highest incidence of those with paralysis was in September and October. Strains of Coxsackie virus were recovered from 5 of the 13 non-paralytic patients tested. One of these strains was neutralised by serum from 10 of the non-paralytic patients, including 5 from which the Coxsackie virus was recovered. Specimens of the same 13 patients were also tested for the presence of poliomyelitis virus. The results were positive from only two of the patients whose faeces did not yield the Coxsackie virus. Curnen came to the conclusion that in individual cases of Coxsackie virus infection presenting with clinical features of aseptic meningitis, it was not possible on the basis of clinical observation alone to differentiate from non-paralytic poliomyelitis.

It is submitted therefore, that the evidence quoted supports the findings described in this thesis that many cases previously diagnosed as non-paralytic poliomyelitis were, in fact, acute infective encephalitis due to other neurotropic viruses.

Only cases of the benign meningitic syndrome are discussed here. Cases of benign myalgic encephalomyelitis such as described by Ramsay and O'Sullivan (Lancet 1956) and also the outbreaks at the Royal Free Hospital, Gray's Inn Road, London, amongst the nurses (Lancet 1955) are not included in this discussion. The term acute infective encephalitis is applied to the outbreaks at Bourn and at Bishop's Stortford.

Various other terms are used in the nomenclature of such diseases including aseptic meningitis, virus encephalitis and lymphocyte meningitis. The advantage of using the term acute infective encephalitis is that it describes, with some accuracy, the clinical entity.

The disease is certainly acute. There is little doubt about its infectivity and it is certainly encephalitic. This title also has the advantage that it brings the condition within the scope of diseases which a general practitioner is under obligation to notify to the local medical officer of health in England and Wales. Although the term aseptic meningitis, virus encephalitis, and lymphocytic meningitis, could be applied to these outbreaks, they are not notifiable diseases.

There is little doubt that the great majority of such diseases are due to neurotropic virus infections. Sporadic cases occur occasionally which may be due to other diseases, as, for example, leptospirosis, and it would therefore seem out of place to use the term virus encephalitis generally.

The community at Bourn consisted of 90 individuals, both adults and children. They lived on a disused aerodrome site one mile from the main village of Bourn, which is six miles from Cambridge. The population of the village in the 1951 census was 1053. It could be taken therefore, as being about 1100 in 1955. There is a small school on the aerodrome site which the children of school age attend.

In this isolated community there occurred eight cases of infective encephalitis, and three cases occurred in each of two separate households. Two nurses who attended the original cases admitted to Addenbrooke's Hospital, together with the husband of one of the nurses, were also infected. It is, therefore, obvious that the infectivity rate was of a high order.

The second group of cases of infective encephalitis came from Bishop's Stortford. This is a town with a population of approximately 13,000 inhabitants. Of the ten cases admitted under my care, two members of the same family were

infected in two instances. All the children of school age attended the same school. The infectivity rate was therefore considerable.

Little information is available regarding the epidemiology of the 50 cases of acute non-paralytic poliomyelitis described, for they occurred over a number of years from 1947 - 1953.

In no instance, however, in the 200 cases of paralytic and non-paralytic acute poliomyelitis considered in this survey did there occur an instance in which more than one member of the same family was proved to be suffering from acute poliomyelitis. There occurred various instances in which there was a history of an illness in other members of the family within a period of weeks. In many cases this was not, however, of sufficient severity to warrant either the advice of the family doctor or admission to hospital.

One point of differentiation, therefore, in the epidemiology of acute poliomyelitis and these two other epidemics, is that the morbidity rate of the outbreaks at Bourn and Bishop's Stortford were of a much high order than that found in acute poliomyelitis.

In both the Bourn and Bishop's Stortford outbreaks an important point to be considered was whether or not they could be due to acute non-paralytic poliomyelitis.

The first two admissions from Bishop's Stortford were C.J.B. and S.B., brother and sister. This factor alone, and also the fact that two days later D.B., a cousin living in the adjacent house, was admitted with a similar illness, would seem to be in favour of an infection other than acute poliomyelitis.

The sequence of seven admissions from this area within ten days of the first admissions all with a similar clinical picture and none with paralysis, made the diagnosis of acute non-paralytic poliomyelitis most improbable.

Let us consider the early admissions to Brookfields Hospital from Bourn, and discuss what in the history of such cases could help us to decide whether or not they could be non-paralytic poliomyelitis. The first admission from the Bourn settlement was that of M.M., a girl of 12 years of age, admitted on the 28th October, 1955. A history of contact with two cases of "meningitis" occurring in the area within the previous week was obtained. Further enquiry revealed that two cases, M.B. and R.C., had been admitted to another hospital (Addenbrooke's Fig. 10) on the 22nd and 26th

October respectively. They had been diagnosed as suffering from virus encephalitis. They were discharged home after a few days, M.B. being discharged on the 25th October and the other R.C., on the 28th.

The position, therefore, from the epidemiological aspect at the time of this first admission to Brookfields Hospital on the 28th October, was that this was the third case of acute encephalitis without paralysis occurring, within a week, in this small community. The occurrence of three cases of acute encephalitis, none of whom had any paralysis would indicate that the diagnosis of acute poliomyelitis was most unlikely.

In the following 14 days further cases suffering from acute encephalitis, none of which had any paralysis, were admitted from the same community. On epidemiological considerations alone it appeared certain that this outbreak was not due to that of acute poliomyelitis.

As regards the symptoms and clinical findings in the three different groups, the poliomyelitis group, the Bourn, and Bishop's Stortford group, there is little of a positive nature to differentiate them. Headache, backache, and vomiting were prominent symptoms in all three.

In the case of the Bourn outbreak there was a biphasic element in the onset of only one case, namely that of E.K. The temporary improvement in this patient's condition was, however, very definite, she was well enough to get up, cycle to visit her mother at some distance from her home, spend the day with her, and later cycle back to her home in the evening. There was a return of her symptoms on the following day.

In the Bishop's Stortford epidemic there was a history of a prodromal illness in 40% of the cases admitted under my care. These symptoms consisted of headache and sore throat. In two of the cases vomiting occurred.

A history of prodromal illness was obtained in 44% of the cases of acute poliomyelitis.

A biphasic pattern in the history was therefore the common factor in 44% of the poliomyelitis group and 40% of the Bishop's Stortford group.

Meningism was a feature in all groups. The degree of meningism in the case of the Bourn and Bishop's Stortford outbreaks was more marked than in the majority of the poliomyelitis group. Vomiting was also a more persistent feature in the case of the Bourn and Bishop's Stortford groups.

This study of the epidemiological pattern was of help in coming to a diagnosis as to whether or not the early admissions in both the Bourn and Bishop's Stortford outbreak were non-paralytic poliomyelitis. The outbreaks at Bourn and Bishop's Stortford occurred during the seasonal period of prevalence of acute poliomyelitis.

Changes in the cellular content of cerebrospinal fluid were found in all cases examined in the combined Bourn and Bishop's Stortford groups. In the poliomyelitis group 11% showed no change as regards cells or protein.

With regard to the type of cell found there is a certain degree of similarity between the poliomyelitis group and the Bishop's Stortford group, in that 15% of the poliomyelitis group revealed a preponderance of granulocytes over lymphocytes. In 22% of the Bishop's Stortford group a preponderance of granulocytes occurred. In each instance a lumbar puncture was performed within four days of the onset of the illness.

On the other hand, in the Bourn group lymphocytes predominated throughout. A further point of similarity between the poliomyelitis group and the Bishop's Stortford group is that there was a biphasic pattern in the history of onset in 44% and 40% respectively.

In the epidemiology of the Bourn and Bishop's Stortford outbreak, the high incidence of the disease among close contacts is a striking feature. For example, in the Bourn epidemic three members of two separate households became infected. Two nurses in a general hospital, both contacts, became infected, and the husband of one of them.

At Bishop's Stortford a brother and sister were infected and also a mother and daughter, two members in each of two separate families out of a total of 10 cases admitted to Brookfields Hospital.

This high infectivity rate is in contrast to that of the poliomyelitis group. There is no doubt that more than one of acute poliomyelitis can occur in the same family. This happened in the case quoted by Krill and Toomey (1941) in which five of six children of the same family had tonsillectomy performed on 22nd August. By 7th September all five had developed bulbar poliomyelitis, and three of them died within two days.

Of the 200 cases of acute poliomyelitis admitted under my care to Brookfields Hospital, there were only two occasions on which two members of the same family were admitted. In neither family was there any evidence of clinical infection

with poliomyelitis in the second admission. In the first case the father suffered from paralytic poliomyelitis. His son was admitted with a raised temperature, but was not meningeal and had no neurological abnormality. Lumbar puncture showed no abnormality. This may have been abortive poliomyelitis, but virus investigations were not then possible.

In the other instance, a brother and sister were admitted. The brother had a flaccid paralysis of his right arm, with cerebrospinal fluid changes. The provisional diagnosis of acute poliomyelitis was confirmed. The sister, aged three years, was admitted because of a history of pyrexia and malaise and no neurological abnormality was found. All investigations including lumbar puncture were negative. The patient was detained in hospital for seven days and discharged quite fit with no definite diagnosis being possible. It is not unreasonable on this evidence alone to suggest that the occurrence of more than one case of clinical poliomyelitis in one family is very uncommon.

The occurrence of a sequence of cases of acute infective encephalitis, as defined in this thesis, without any cases with paralysis, is another factor that could raise doubts as to whether we were dealing with acute poliomyelitis.

In the past the diagnosis of non-paralytic poliomyelitis has been a matter of epidemiological probability. When cases occurred with the syndrome of acute aseptic meningitis, i.e., meningism, pleocytosis in the cerebrospinal fluid (for which other causes could be excluded) in an area in which paralytic poliomyelitis was prevalent, one felt justified in making a diagnosis of acute poliomyelitis. Although the Bourn and Bishop's Stortford outbreaks occurred during the period of seasonal prevalence of acute poliomyelitis in this area, virus investigations demonstrated that the disease was not poliomyelitis. In the Autumn of both 1955, when the Bourn epidemic occurred, and in the Autumn of 1956, when the Bishop's Stortford outbreak occurred, a considerable number of cases of acute poliomyelitis were admitted to Brookfields Hospital. The number of admissions of paralytic and non-paralytic patients and also the number of cases of post-infective encephalitis and of virus encephalitis of unknown origin, is shown in Fig. 15.

The Ministry of Health Annual Report of notifications of paralytic and non-paralytic paralysis for the years 1950-1955 are tabulated in Fig. 16.

FIGURE 15.

YEAR	POLIOMYELITIS		POST-INFECTIVE ENCEPHALITIS	VIRUS ENCEPHALITIS
	PARALYTIC	NON-PARALYTIC		
1947	20	7	-	-
1948	4	-	-	-
1949	35	15	2	-
1950	15	5	1	-
1951	36	13	5	1
1952	37	12	5	1
1953	54	18	4	2
1954	2	7	1	6
1955	28	16	1	22
1956	21	11	3	21
TOTAL	252	104	22	53

FIGURE 16.

YEAR	POLIOMYELITIS	
	PARALYTIC	NON-PARALYTIC
1950	5565	2195
1951	1529	1085
1952	2747	1163
1953	2976	1571
1954	1319	641
1955	3712	2619

This shows that for the six-year period under review, the number of paralytic notifications has outnumbered the non-paralytic notofications in proportions varying from 5 to 2 in 1950 amd 1952, to 3 to 2 in 1951 and 1956. Separate notifications of paralytic, as distinct from non-paralytic, poliomyelitis were required by the Ministry of Health for the first time in 1950.

The rate of paralytic to non-paralytic cases in the Ministry of Health Returns and the Brookfields Hospital figures are roughly the same, about 2 to 1 in the case of former figures and $2\frac{1}{2}$ to 1 in the latter. The higher figures for Brookfields Hospital are accounted for by the higher ratio of paralytic to non-paralytic up to 1953. It is possible that this can be explained by the fact that more cases of non-paralytic poliomyelitis were recognised in the latter years.

The figures quoted by Lassen during the severe epidemic of poliomyelitis in Denmark in the Winter of 1952, shows a different pattern (Lassen 1953). In this epidemic there occurred 866 paralytic and 1856 non-paralytic cases. This ratio of paralytic to non-paralytic is the reverse of the figures for England and Wales, and also the reverse of my

own figures for Brookfields Hospital. The number of cases of non-paralytic poliomyelitis notified in Denmark is four times that to be expected according to the Ministry of Health statistics for a six-year period and the smaller number occurring at Brookfields Hospital over a ten-year period.

There would seem to be three possible explanations for this:-

1. That during a widespread epidemic, such as occurred in Denmark in 1952, both the general population and the medical profession were more aware of the possibility of its occurrence, and therefore many more such cases were diagnosed.

2. That many of the cases notified as non-paralytic poliomyelitis might have been due to a neurotropic virus (not poliomyelitis) producing a clinical picture similar to that of non-paralytic poliomyelitis as in fact occurred in the Bishop's Stortford and Bourn outbreaks which have been described.

3. That one particular strain of poliomyelitis virus was predominant during the Danish epidemic. I can find no report that virus investigations to prove or disprove this possibility were done in Denmark. It is, indeed, doubtful

whether resources to undertake such an investigation were possible at that time when the growth of poliomyelitis virus on tissue culture was in its early stages of development.

With regard to the first possible explanation of the unexpected high ratio of non-paralytic to paralytic cases in the Danish outbreak, there is little doubt that increased numbers of non-paralytic cases are recognised during an epidemic. To what extent this occurs must be a matter of surmise.

Let us consider what evidence there is of other possible factors concerned. It will be seen from a study of Fig. 14 that the number of paralytic poliomyelitis admissions to Brookfields Hospital in each year from 1947 to 1953 outnumbered the non-paralytic admissions by 3 to 1. The total of paralytic cases for the period being 201 as compared with 70 non-paralytic cases. During this same period only four cases of benign virus encephalitis were admitted.

In 1954 only two cases of paralytic poliomyelitis were admitted. It is significant that in that year seven cases were admitted which were diagnosed as non-paralytic poliomyelitis. One was admitted in July, three in September, One in October and two in November. Of the two paralytic

poliomyelitis cases, one was admitted in July and the other in September. Of the six cases diagnosed as virus encephalitis in 1954, two were admitted in January, May and June respectively. As there was no paralytic poliomyelitis in the area at that time, they were regarded as due to an unidentified neurotropic virus. Virus investigations of these cases were not possible at that time. We have, therefore, a total of 13 cases indistinguishable clinically from non-paralytic poliomyelitis and two cases of paralytic poliomyelitis admitted to Brookfields Hospital in 1954.

In 1955 and 1956 when 44 and 32 cases of poliomyelitis were admitted, the ratio of paralytic to non-paralytic was about the average ratio for England and Wales, nearly 2 to 1. There was, however, a further increase in the number of virus encephalitis cases admitted for both of these years, 22 in 1955 and 21 in 1956.

Of the 22 cases of virus encephalitis admitted in 1955, complete virus investigation was possible only in the eleven cases admitted from Bourn. Poliomyelitis virus isolation was negative in all of them. Coxsackie virus investigations were also negative.

Poliomyelitis virus investigation only was done in 18 of the 21 cases diagnosed as virus encephalitis in 1956. Poliomyelitis virus was not isolated from any of the 18 investigated.

It is apparent, therefore, that there is a relative increase for the years 1954, 1955 and 1956, in the number of cases of virus encephalitis. These cases were clinically indistinguishable from non-paralytic poliomyelitis.

In 1955 and 1956 this increase occurred at the time of seasonal prevalence of poliomyelitis and when a considerable number of cases of acute poliomyelitis were admitted.

The result of the virus investigation on the Bourn group, and the fact that faeces from 18 of 21 cases in the 1956 group failed to grow poliomyelitis virus, seems conclusive evidence that neurotropic viruses other than poliomyelitis produced clinical entities simulating non-paralytic poliomyelitis.

SUMMARY

The occurrence of two epidemics of benign infective virus encephalitis in 1955 and 1956, in the Cambridge area, has been described and compared with a series of cases of non-paralytic poliomyelitis.

It was not found possible to establish a differential diagnosis in individual cases as a result of clinical findings alone, but a study of the epidemiological pattern was of considerable help in the differentiation of the three main groups of cases described.

Virus investigations proved that the Bourn epidemic was due to Type 9 of the E.C.H.O. group of viruses. This virus work was carried out by Dr. Donald M. McLean, at that time Harrison Watson Student, Clare College, Cambridge. Poliomyelitis virus investigations of the Bishop's Stortford cases were done by members of the Regional Public Health Laboratory, Cambridge.

The cases on which the findings in this thesis are based were admitted to Brookfields Hospital, Cambridge, the infectious diseases unit of the United Cambridge Hospitals, of which I am Physician-in-Charge. A list of references is appended.

It is submitted that epidemics of acute infective encephalitis are becoming increasingly prevalent in recent years. In some instances these occur simultaneously with cases of acute poliomyelitis.

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